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Human and Animal Transmissible Spongiform Encephalopathies including Bovine Spongiform Encephalopathy

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Introduction

Bovine Spongiform Encephalopathy (BSE) belongs to a family of diseases called Transmissible Spongiform Encephalopathies or TSE's. Encephalopathies are diseases of the brain. Spongiform comes from the fact that the brain takes on the structure of a sponge and transmissible means the disease can be spread. TSE's are classified as:

- Sporadic, which means it occurs somewhat randomly, and the cause is unidentified.
- Familial or inherited, which means it is passed on genetically from parents to offspring.
- Acquired, which means the source of the disease is from outside the animal.
- Iatrogenic, which is a special form of acquired and means it is spread through medical procedures

All TSE's are diseases of the central nervous system and slowly cause its failure. All have long incubation periods lasting from months to years. There is no cure and they are always fatal.

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Human TSE's

TSE's affect both people and animals. Most human TSE's are sporadic or inherited. However, with the BSE outbreak in the United Kingdom and its spread to other countries, plus the strong evidence of a BSE link to the human disease variant Creutzfeldt-Jakob disease (vCJD), the public's interest in this class of diseases has increased. The only indication of horizontal spread of human TSE diseases is through medical procedures and in the disease Kuru, both acquired TSE's.

About 80% of the human TSE cases are Creutzfeldt-Jakob disease (CJD). CJD generally affects people in the 45 to 75 year age range. It occurs sporadically throughout the world at a rate of 1 case per 1 to 2 million people.

People live about 4 to 5 months after clinical signs of the disease appear. There is also documentation of this disease being spread through medical procedures

Fatal Familial Insomnia (FFI) was first described in 1986 and runs in families. Just as the name implies the victims have a sleep disorder which results in death. A second inherited human TSE is Gerstmann-Straussler syndrome (GSS). This disease was first reported in 1928. GSS usually affects people in their 30's or 40's and results in death within about five years of onset.

Scientists studying scrapie in sheep during the 1950's, became interested in Kuru. This disease affected Fore speaking people in Papua New Guinea. Tribal folklore described the disease as early as the 1920's. It affected people from 5 years of age to over 60 years of age and the illness lasted around 1 year. Eventually it was figured out that it was being transmitted by ritualistic cannibalism.

The first three known cases variant Creutzfeldt-Jakob disease (vCJD) occurred in 1995. Most people that have contracted the disease are in their teens to 30's. The duration of the disease after clinical diagnosis is from 7 to 23 months. As with all TSE's, vCJD always results in death. Clinical signs include anxiety, depression, withdrawal and behavioral changes. So far all cases have been found in Europe except for one case in Hong Kong and a probable case in the U.S. Both women lived in the U.K. for significant amounts of time during the U.K. BSE epidemic.

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Animal TSE's

Animal Transmissible Spongiform Encephalopathies include scrapie, transmissible mink encephalopathy, chronic wasting disease, feline spongiform encephalopathy, and bovine spongiform encephalopathy. Scrapie in sheep and goats has been identified since the 1700's. There is no known human health effect linked to scrapie. The effects on people are economic and political; that is production loss, market loss due export restrictions and possible consumer reaction. Scrapie is believed to be spread both maternally and horizontally through contact with or consumption of placenta. It affects sheep in most major sheep producing countries, with the exception of Australia and New Zealand. Washington State and the United States Departments of Agriculture have had scrapie elimination programs in place for several years.

Transmissible Mink Encephalopathy (TME) occurs in farm-raised mink. It is transmitted by feed and cannibalism. It has been found in North America and Europe but interestingly not in the United Kingdom where both scrapie and BSE are wide spread.

Chronic Wasting Disease (CWD) affects both farm-raised and wild populations of deer and elk. It affects herds in Canada, Colorado, Montana, Nebraska, Oklahoma, South Dakota, Wisconsin, and Wyoming. Washington State Department of Fish & Wildlife has been sampling deer and elk since 1995. During the 2001 hunting seasons the sampling effort was increased and over 720 samples were collected in Washington. All of samples have been negative for CWD upon immunohistochemical analysis.

Bovine Spongiform Encephalopathy (BSE) was first discovered during 1986 in the United Kingdom. Since then it has spread to at least 20 countries. All of the cases in native-born cattle were in Europe until September 2001, when Japan announced their first case. It appears that cats (domestic and large), kudu and nyala also can contract BSE.

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Cause of TSE's
The cause of TSE's is still not fully understood and is subject to research and much debate in the scientific community. The agent that causes TSE's is smaller than the smallest known virus. There is no detectable immune or inflammatory response.

The causative agent is highly resistant to chemical disinfectants. Infectivity has remained after heating to 680^{o} F with dry heat. Steam is more effective than dry heat in reducing infectivity, but even pressurized steam will not totally eliminate the infectivity of the TSE causative agent. The recommended sterilization process for surgical instruments is so harsh that it is hard to find instruments that will stand up to sterilization. Even the recommended sterilization process may not be totally effective.

The causative agent apparently can retain infectivity in the environment for long periods of time. One experiment with brain tissue from hamsters infected with scrapie reports that infectivity was reduced, but not eliminated, by burial in the earth for 3 years.

The three main theories of the causative agent are that it is a virus, a prion, or a virion. A virus is a small piece of genetic material, either deoxyribonucleic acid (DNA) or ribonucleic acid (RNA), surrounded by a protein coat. A prion is small normally occurring protein, without any genetic material, that becomes pathogenic when it changes shape. A virion has a small amount of genetic material and is somewhere between the virus and the prion.

The most widely accepted theory is that the causative agent is a prion. Something introduces an abnormal prion and the abnormal prion affects normal prions that are next to it causing them to change shape. After being converted to this abnormal structure the prion proteins become resistant to the body's usual methods for taking apart misshaped proteins. The newly formed abnormal prions then accumulate and join together in sheets causing the brain or nerves to take on a sponge like appearance.

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BSE and vCJD Relationship
The prion protein found in vCJD and BSE are indistinguishable. The same prion protein is also found in cats with feline spongiform encephalopathy (FSE) and in Kudu and Nyala with TSE. Cats, Kudu and Nyala acquire their diseases after eating infective brain tissue from cattle with BSE.

During 1986 BSE was first identified as a new disease, with just a few animals being affected in the United Kingdom. By 1992 there were 37,280, in 2001 there were 1,019.The total number of BSE cases in the U.K. from 1986 through 2001 was 181,864. (See figure 1 below.)

In 1995 new variant Creutzfeldt-Jakob disease (nvCJD) was recognized as a separate disease and it also originated in the United Kingdom. Later "new" was dropped from the name in most literature and it is now usually known as variant Creutzfeldt-Jakob disease (vCJD). During the first year there were 3 cases identified, in 2001 – 20 cases. There were a total of 113 confirmed and probable cases in the United Kingdom through December 2001. All of the known cases of vCJD have been in Europe, except a woman in Hong Kong and a woman in the U.S., both which had previously lived in Europe.

No one is sure how long the incubation period is for vCJD, but one study done on a cluster of 5 people in North Leicester region of the United Kingdom suggests it is 10 to 16 years. So far all of the people that have died with vCJD have the same genetic trait - double methionine at codon 129 on the prion protein gene. In sheep, it is clear that different genetics determine the length of the incubation period for scrapie. The question then is, if people are not homozygous for methionine at codon 129 on the prion protein gene, are they resistant or just

have a longer incubation period? Predictions for the future number of people to be affected by vCJD range from fewer than one hundred to hundreds of thousands. Most current predictions lean towards the lower end of the scale.

There is strong evidence that vCJD is caused from consuming infective material from cattle with BSE. This has not been proven because of ethical considerations of conducting experiments on people.

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Specified Risk Material
In animals or people with any of the TSE's abnormal prion protein has only been found in certain parts of the body. The specific parts containing abnormal prions vary from species to species. The parts that contain the abnormal prion proteins are termed "Specified Risk Material" (SRM).

In countries where BSE is endemic, the specified risk material (SRM) from cattle is banned from human consumption. The brain, the trigeminal ganglia, (a nerve junction within the head), the eye, the dorsal root ganglia (nerve junctions along the backbone), bone marrow in large bones, and the distal ileum (the last portion of the small intestine) have been shown to contain infective material and are identified as SRM. The abnormal prion protein thought to cause BSE has never been found in milk, hides, or skeletal muscle of food producing animals.

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Testing for TSE's
Currently all tests for BSE require brain tissue. There are no live animal tests for BSE, vCJD, or most of the other TSE's. Scientists are trying to develop a live animal test. The most promising live animal tests for BSE and vCJD at the present time involve using urine or spinal fluid. In sheep, scientists can test the third eyelid for scrapie prions. Sheep test results so far show that 100% of the animals that test positive with the third eyelid test developed scrapie within two years. However, 10 to 15% of those testing negative, also develop scrapie within two years. Scientists have also developed a test for CWD in deer and elk using tonsils.

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Protective Steps by U.S. Government
To protect the U.S. from the introduction and amplification of BSE, the United States Department of Agriculture (USDA) and the Food and Drug Administration (FDA) have taken several steps. These actions are listed below by date.

1986
BSE identified in Great Britain as a new and separate disease.

1987
BSE made a reportable disease in the United States. Suspect cases are to be reported by local veterinarians to the State Veterinarian, and the United State Department of Agriculture, Animal Plant Health Inspection Services (USDA - APHIS) Veterinarian.

1989
Importation of live ruminants and most ruminant products from countries where BSE is known to exist in native cattle is prohibited.

1990
Active USDA surveillance program for BSE began. Cattle that exhibit signs of central nervous system disease are targeted. For details of activities see the USDA APHIS BSE Surveillance website at http://www.aphis.usda.gov/oa/bse/bsesurvey.html.

1997
- Importation of live ruminants and most ruminant products from all of Europe prohibited.
- Feed rule issued that prohibits the use of most mammalian proteins as feed for ruminants. (This rule is currently under review by the Food and Drug Administration (FDA).)

1998
- Quarantine of 3 sheep flocks imported from Europe with possible exposure to BSE. For further information on the outcome of the sheep, visit USDA, APHIS, Veterinary Services TSE In Vermont Sheep website at http://www.aphis.usda.gov/oa/tse/index.html
- BSE surveillance of cattle intensified.
- Inspections at renderers, feed mills, protein blenders, feed haulers, and farms for compliance with BSE feed rule began.

2000
Importation of all rendered animal protein from 31 countries is prohibited. These countries are either known to have BSE in their cattle, or because of inadequate preventive measures within their countries, are considered to present undue risk for introducing BSE into the United States.

2001
- USDA surveillance program for BSE expanded to include all cattle that are non-ambulatory at slaughter.
- Importation of live ruminants, ruminant meat, meat products and other ruminant protein products from Japan prohibited.

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U.S. Feed Rule
The 1997 feed rule, title 21 CFR589.2000, prohibits the feeding of all mammalian protein to ruminants except for milk products, blood products, gelatin, pure porcine (hog) and pure equine (horse) and plate waste. Below is a brief discussion about each of these exempted products. Some of these exempt products are being revaluated as part of the current rule review process.

Milk Products – Milk from cows with BSE has been fed, injected parenterally (outside the blood stream) and intracranially (within the skull) in calves, mice and other species and has never caused BSE in those animals. There is no evidence to date that BSE is transmitted through milk.

Blood Products – The same tests have been conducted with blood with no BSE resulting. However, there is much debate about the possibility of contamination of the blood products during slaughter. Therefore, the safety of blood products is somewhat debatable. However, considering that no BSE has ever been found in the U.S., at this time the feeding of blood products is allowed.

Gelatin – There appears to be adequate control of material sources and reduction of possible infectivity through processing given our countries BSE status. One major source of gelatin is hides. Hides have never been shown to contain abnormal prion proteins.

Pure Pork and Pure Horse –Pigs have contracted BSE after being injected with infective material. However, neither pigs nor horses have contracted any TSE from eating infective material.

Plate waste or as the rule says "inspected meat products, cooked and offered for human food and further heat processed." The argument has been, if it is OK for people to eat, why wouldn't it be OK for ruminants. However, there is quite a bit of debate over the safety of plate waste.

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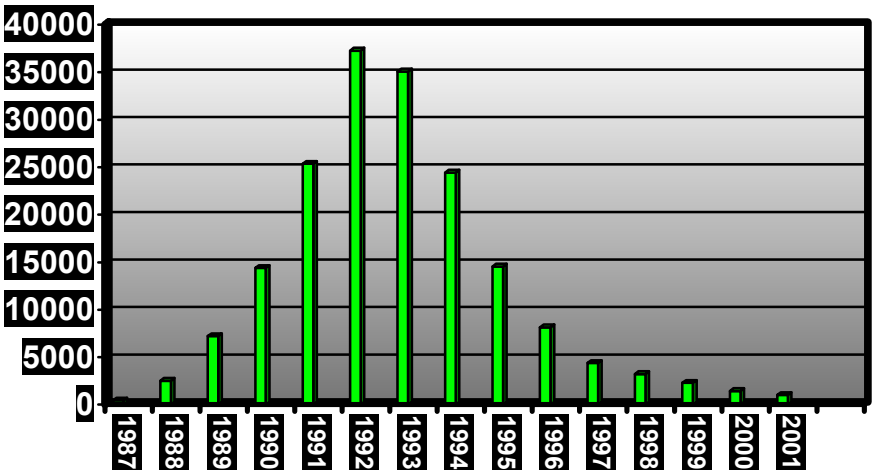

Data from Office International Des Epizooties

Figure 1. The number of cases of BSE in Great Britain by year from 1987 to 2001

In 1988 the UK prohibited feeding certain animal proteins to ruminants. It took some time to get compliance and the rule has been tightened up several times since it was first implemented.

There is a 2 to 8 year incubation period for BSE from the time of consumption of the infective material until clinical signs appear.

Just 4 years after the feed ban was implemented, the number of new cases of BSE peaked and began a dramatic decline. It appears the feed ban has been extremely effective at controlling BSE in the UK.

The USDA/Harvard BSE Risk Assessment released November 2001, identified the feed ban as the main reason a BSE epidemic would not occur in the United States even if there were BSE positive animals here. It is very important for ruminant producers to follow the feed ban.

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Surveillance for BSE
Since 1990 USDA has been actively looking for BSE in the U.S. The program has targeted cattle that exhibit central nervous system disorders. Other countries claim we have not found BSE in the U.S. because we are not looking hard enough. Therefore USDA has responded and broadened their sampling target. Now they are sampling all cows that they can find that are down, regardless of the reason they are down. The greater number of animals now being tested results in only a slight increase in the chances of finding an animal with BSE.

Being able to say, based on an active surveillance program, that we have not found any cases of BSE is worth millions of dollars every year to the cattle industry. During Federal fiscal year 2001, 5245 samples were checked. In the first five months of the 2002 fiscal year 6084 samples were tested.

In 1998 USDA contracted with the Harvard Center for Risk Analysis, Harvard University, to evaluate the strength of measures in place to prevent the spread of BSE to cattle and/or humans if it should occur in the U.S. Their analysis concludes, "… the U.S. is highly resistant to any introduction of BSE or a similar disease. BSE is extremely unlikely to become established in the U.S. For example, in a hypothetical scenario in which ten cattle infected with BSE are imported into the U.S., on average only three new cases of BSE would occur. Moreover, the disease is virtually certain to be eliminated from the country within 20 years after its introduction."

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Response Plan
In the early 1990's FDA and USDA developed a response plan in case BSE is found in the U.S. This plan had major revisions to it from 1996 through 1998. It is currently under revision again. As we learn more and as personnel change the plan is revised, so that people know what they are to do in the event BSE occurs. Under the current plan, if a case of BSE should be suspected in the U.S., a private veterinary is to contact a State or Federal Veterinarian. If the government veterinarian suspects BSE, they would make arrangements for obtaining a brain tissue sample and send the sample to a Federal Lab. If the Federal Lab decides it looks like BSE the sample will be hand carried to the UK for confirmation. In the mean time, the farm would be put under quarantine, and feed and animals entering and leaving the farm for the past several years would be traced. If BSE is confirmed, then the herd will be purchased and destroyed by the government.

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Producer Preventative Actions
As a ruminant producer you can help prevent BSE by:

1. Looking for and obeying the cautionary statement "**Do Not Feed Cattle or Other Ruminants**" on feed labels. Poultry and swine feed frequently contain materials that are prohibited for ruminants. Some horse products also contain prohibited materials. If feed for these, or any other species except pets, contains any of the prohibited materials, then they are to be labeled with the cautionary statement and must not be fed to ruminants. Pet food is exempt from this labeling requirement.

2. Do not allow ruminants access to pet food. Dogs and cats are carnivores. Pet food is advertised as containing real meat, so be aware that Pet Food often contains prohibited materials and therefore ruminants should not have access to it. Pet food labeling does not contain the cautionary statement. Avoid feeding cats and dogs where spilled pet food will be mixed with hay or other ruminant feed. Store dog food where if a goat gets out it cannot into the dog food, etc.

3. Avoid cross-contamination. Do not use the same pail or feeding equipment to handle feed for ruminants that is used to feed non-ruminants if the non-ruminant feed contains prohibited material. If you receive bulk grain shipments, ask the truck driver what the previous load was so they become more aware of the potential of them contaminating ruminant feed with prohibited material.

4. Title 21 CFR 589.2000 requires ruminant producers to keep records of any feeds fed containing any animal protein, regardless of specie fed, excluding pet food fed to pets. These records include purchase invoices and feed labels from each lot of feed. The invoices should show the product name, date, quantity and supplier. These records are to be kept for a minimum of 1 year.

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For further information visit the BSE page on the Washington State Department of Agriculture internet site: http://agr.wa.gov/pmd/feeds/bse.htm . You may also contact Neil Lanning at nlanning@agr.wa.gov or phone 360-902-2052 or Pesticide Management Division, Washington State Department of Agriculture, P.O. Box 42589, Olympia, WA 98504-2589